SAFETY DATA SHEET
Olmesartan / Amlodipine Besylate Formulation

Section 1: Identification

Product name: Olmesartan / Amlodipine Besylate Formulation

Manufacturer or supplier’s details
Company: MSD
Address: 33 Whakatiki Street - Private Bag 908
          Upper Hutt - New Zealand
Telephone: 908-740-4000
Emergency telephone number: 1-908-423-6000
E-mail address: EHSDATASTEWARD@msd.com
Telefax: 908-735-1496

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical

Section 2: Hazard identification

GHS Classification
Reproductive toxicity: Repr.1A

GHS label elements
Hazard pictograms: 

Signal word: Danger
Hazard statements: H360D May damage the unborn child.
Precautionary statements: Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P281 Use personal protective equipment as required.
Response:
P308 + P313 IF exposed or concerned: Get medical advice/
attention.
Storage:
P405 Store locked up.
Disposal:
P501 Dispose of contents/ container to an approved waste
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Date of first issue: 07.01.2016

disposal plant.

Other hazards which do not result in classification
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

Section 3: Composition/information on ingredients

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemical name</td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
</tr>
<tr>
<td></td>
<td>Olmesartan</td>
</tr>
<tr>
<td></td>
<td>Amlodipine Besylate</td>
</tr>
<tr>
<td></td>
<td>Titanium dioxide</td>
</tr>
</tbody>
</table>

Section 4: First-aid measures

General advice: In the case of accident or if you feel unwell, seek medical advice immediately.
When symptoms persist or in all cases of doubt seek medical advice.

If inhaled: If inhaled, remove to fresh air.
Get medical attention.

In case of skin contact: In case of contact, immediately flush skin with soap and plenty of water.
Remove contaminated clothing and shoes.
Get medical attention.
Wash clothing before reuse.
Thoroughly clean shoes before reuse.

In case of eye contact: In case of contact, immediately flush eyes with plenty of water for at least 15 minutes.
If easy to do, remove contact lens, if worn.
Get medical attention.

If swallowed: If swallowed, DO NOT induce vomiting.
Get medical attention.
Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed: May damage the unborn child.
Contact with dust can cause mechanical irritation or drying of the skin.

Protection of first-aiders: First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician: Treat symptomatically and supportively.

Section 5: Fire-fighting measures

Suitable extinguishing media: Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing: None known.
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Specific hazards during firefighting:
Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard. Exposure to combustion products may be a hazard to health.

Hazardous combustion products:
Carbon oxides

Specific extinguishing methods:
Use extinguishing measures that are appropriate to local circumstances and the surrounding environment. Use water spray to cool unopened containers. Remove undamaged containers from fire area if it is safe to do so. Evacuate area.

Special protective equipment for firefighters:
In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

Section 6: Accidental release measures

Personal precautions, protective equipment and emergency procedures:
Use personal protective equipment. Follow safe handling advice and personal protective equipment recommendations.

Environmental precautions:
Discharge into the environment must be avoided. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up:
Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air). Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

Section 7: Handling and storage

Technical measures:
Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation:
If sufficient ventilation is unavailable, use with local exhaust ventilation.

Advice on safe handling:
Do not get on skin or clothing. Do not breathe dust.
Do not swallow.
Do not get in eyes.
Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment
Keep container tightly closed.
Minimize dust generation and accumulation.
Keep container closed when not in use.
Keep away from heat and sources of ignition.
Take precautionary measures against static discharges.
Take care to prevent spills, waste and minimize release to the environment.

Hygiene measures : If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place.
When using do not eat, drink or smoke.
Wash contaminated clothing before re-use.
The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

Conditions for safe storage : Keep in properly labelled containers.
Store locked up.
Keep tightly closed.
Store in accordance with the particular national regulations.

Materials to avoid : Do not store with the following product types:
Strong oxidizing agents

Section 8: Exposure controls/personal protection

Components with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>WES-TWA</td>
<td>10 mg/m³</td>
<td>NZ OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Olmesartan</td>
<td>144689-63-4</td>
<td>TWA</td>
<td>30 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>300 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Amlodipine Besylate</td>
<td>652969-01-2</td>
<td>TWA</td>
<td>20 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>100 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>WES-TWA</td>
<td>10 mg/m³</td>
<td>NZ OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³ (Titanium dioxide)</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

Engineering measures : All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment. Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices).
Minimize open handling.

**Personal protective equipment**

**Respiratory protection**: If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

- **Filter type**: Particulates type
- **Hand protection**: Chemical-resistant gloves

**Remarks**: Consider double gloving.

**Eye protection**: Wear safety glasses with side shields or goggles. If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles. Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

**Skin and body protection**: Work uniform or laboratory coat. Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces.

Use appropriate degowning techniques to remove potentially contaminated clothing.

**Section 9: Physical and chemical properties**

- **Appearance**: powder
- **Colour**: No data available
- **Odour**: No data available
- **Odour Threshold**: No data available
- **pH**: No data available
- **Melting point/freezing point**: No data available
- **Initial boiling point and boiling range**: No data available
- **Flash point**: Not applicable
- **Evaporation rate**: Not applicable
- **Flammability (solid, gas)**: May form explosive dust-air mixture during processing, handling or other means.
- **Flammability (liquids)**: No data available
- **Upper explosion limit / Upper flammability limit**: No data available
- **Lower explosion limit / Lower flammability limit**: No data available
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flammability limit
Vapour pressure : Not applicable
Relative vapour density : Not applicable
Relative density : No data available
Density : No data available
Solubility(ies)
Water solubility : No data available
Partition coefficient: n-octanol/water : Not applicable
Auto-ignition temperature : No data available
Decomposition temperature : No data available
Viscosity
Viscosity, kinematic : Not applicable
 Explosive properties : Not explosive
Oxidizing properties : The substance or mixture is not classified as oxidizing.
Particle size : No data available

Section 10: Stability and reactivity
Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reactions : May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.
Conditions to avoid : Heat, flames and sparks.
 Avoid dust formation.
Incompatible materials : Oxidizing agents
Hazardous decomposition products : No hazardous decomposition products are known.

Section 11: Toxicological information
Exposure routes :
Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity
Not classified based on available information.

Product:
Acute oral toxicity : Acute toxicity estimate: > 2,000 mg/kg
Method: Calculation method

**Components:**

**Cellulose:**
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
- Acute inhalation toxicity: LC50 (Rat): > 5.8 mg/l  
  Exposure time: 4 h  
  Test atmosphere: dust/mist
- Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg

**Olmesartan:**
- Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg  
  LD50 (Mouse): > 2,000 mg/kg  
  LD50 (Dog): > 1,500 mg/kg
- Acute inhalation toxicity: Remarks: No data available
- Acute dermal toxicity: Remarks: No data available

**Amlodipine Besylate:**
- Acute oral toxicity: LD50 (Rat): 393 mg/kg

**Titanium dioxide:**
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
- Acute inhalation toxicity: LC50 (Rat): > 6.82 mg/l  
  Exposure time: 4 h  
  Test atmosphere: dust/mist  
  Assessment: The substance or mixture has no acute inhalation toxicity

**Skin corrosion/irritation**
Not classified based on available information.

**Components:**

**Olmesartan:**
- Remarks: No data available

**Titanium dioxide:**
- Species: Rabbit
- Result: No skin irritation

**Serious eye damage/eye irritation**
Not classified based on available information.
Components:

Olmesartan:
Species: Rabbit
Result: Moderate eye irritation
Method: Draize Test

Amlodipine Besylate:
Species: Rabbit
Result: Severe irritation

Titanium dioxide:
Species: Rabbit
Result: No eye irritation

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Olmesartan:
Exposure routes: Skin contact
Remarks: No data available

Titanium dioxide:
Test Type: Local lymph node assay (LLNA)
Exposure routes: Skin contact
Species: Mouse
Result: negative

Chronic toxicity

Germ cell mutagenicity
Not classified based on available information.

Components:

Cellulose:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) Result: negative
Test Type: In vitro mammalian cell gene mutation test Result: negative

Genotoxicity in vivo: Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
Species: Mouse
Application Route: Ingestion
Olmesartan:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) Result: negative

Genotoxicity in vitro: Test Type: Mutagenicity (in vitro mammalian cytogenetic test) Result: negative

Genotoxicity in vitro: Test Type: Chromosome aberration test in vitro Test system: Chinese hamster lung cells Result: positive

Genotoxicity in vivo: Test Type: Mouse Lymphoma Result: negative

Genotoxicity in vivo: Test Type: Micronucleus test Species: Mouse Cell type: Bone marrow Application Route: Oral Result: negative

Germ cell mutagenicity - Assessment: Weight of evidence does not support classification as a germ cell mutagen.

Amlodipine Besylate:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) Result: negative

Genotoxicity in vitro: Test Type: Chromosome aberration test in vitro Result: negative

Titanium dioxide:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) Result: negative

Genotoxicity in vivo: Test Type: In vivo micronucleus test Species: Mouse Result: negative

Carcinogenicity
Not classified based on available information.

Components:
Cellulose:
Species: Rat Application Route: Ingestion Exposure time: 72 weeks Result: negative
Olmesartan:  
Species: Rat  
Application Route: Oral  
Exposure time: 2 Years  
Result: negative

Species: Mouse  
Application Route: Oral  
Exposure time: 6 Months  
Result: negative

Amlodipine Besylate:  
Species: Mouse  
Application Route: Oral  
Exposure time: 2 Years  
Result: negative

Species: Rat  
Application Route: Oral  
Exposure time: 2 Years  
Result: negative

Titanium dioxide:  
Species: Rat  
Application Route: inhalation (dust/mist/fume)  
Exposure time: 2 Years  
Method: OECD Test Guideline 453  
Result: positive  
Remarks: The mechanism or mode of action may not be relevant in humans.

Carcinogenicity - Assessment: Limited evidence of carcinogenicity in inhalation studies with animals.

Reproductive toxicity  
May damage the unborn child.

Components:

Cellulose:  
Effects on fertility: Test Type: One-generation reproduction toxicity study  
Species: Rat  
Application Route: Ingestion  
Result: negative

Effects on foetal development: Test Type: Fertility/early embryonic development  
Species: Rat  
Application Route: Ingestion  
Result: negative

Olmesartan:  
Effects on fertility: Test Type: Fertility
Species: Rat
Application Route: Oral
Fertility: NOAEL: 1,000 mg/kg body weight
Result: No effects on fertility

Test Type: Development
Species: Rat
Application Route: Oral
Dose: 1000 milligram per kilogram
Result: No teratogenic effects

Test Type: Development
Species: Rabbit
Application Route: Oral
Dose: 1 milligram per kilogram
Result: No teratogenic effects

Test Type: Development
Species: Rat
Application Route: Oral
Developmental Toxicity: LOAEL: >= 1.6 mg/kg body weight
Symptoms: Malformations were observed., Reduced body weight
Result: Effects on postnatal development

Reproductive toxicity - Assessment: Positive evidence of adverse effects on development from human epidemiological studies.

Amlodipine Besylate:

Effects on fertility: Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Ingestion
Fertility: NOAEL: 10 mg/kg body weight
Result: No effects on fertility

Test Type: Fertility/early embryonic development
Species: Rabbit
Application Route: Ingestion
Fertility: NOAEL: 25 mg/kg body weight
Result: No effects on fertility

Effects on foetal development: Test Type: Embryo-foetal development
Species: Rat
Application Route: Ingestion
Developmental Toxicity: LOAEL: 10 mg/kg body weight
Result: Effects on foetal development

Test Type: Embryo-foetal development
Species: Rabbit
Application Route: Ingestion
Developmental Toxicity: NOAEL: 10 mg/kg body weight
Result: No effects on foetal development

Test Type: Embryo-foetal development
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Species: Mouse
Application Route: Ingestion
Developmental Toxicity: LOAEL: 1.6 mg/kg body weight
Result: Effects on foetal development
Remarks: Maternal toxicity observed.

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
Not classified based on available information.

Repeated dose toxicity

Components:

Cellulose:
Species : Rat
NOAEL : >= 9,000 mg/kg
Application Route : Ingestion
Exposure time : 90 Days

Olmesartan:
Species : Rat
NOAEL : 2,000 mg/kg
Application Route : Oral
Exposure time : 24 Months
Remarks : No significant adverse effects were reported

Amlodipine Besylate:
Species : Rat
NOAEL : 15 mg/kg
Application Route : Oral
Exposure time : 90 d
Remarks : No significant adverse effects were reported

Titanium dioxide:
Species : Rat
NOAEL : 24,000 mg/kg
Application Route : Ingestion
Exposure time : 28 Days

Species : Rat
NOAEL : 10 mg/m3
Application Route : inhalation (dust/mist/fume)
Exposure time : 2 yr

Aspiration toxicity
Not classified based on available information.
Experience with human exposure

**Product:**
Ingestion: Symptoms: Fatigue, Dizziness, Headache, Nausea

**Components:**

**Olmesartan:**
- Eye contact: Symptoms: Eye irritation
- Ingestion: Symptoms: hypotension Remarks: May cause harm to the unborn child. Based on Human Evidence

**Amlodipine Besylate:**
- Eye contact: Symptoms: Severe irritation
- Ingestion: Symptoms: Nausea, Abdominal pain, Fatigue, Headache, Oedema, Palpitation

**Section 12: Ecological information**

**Ecotoxicity**

**Components:**

**Cellulose:**
- Toxicity to fish: LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l Exposure time: 48 h Remarks: Based on data from similar materials

**Amlodipine Besylate:**
- Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): 2.7 mg/l Exposure time: 96 h
- Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 3.2 mg/l Exposure time: 48 h
- Toxicity to algae/aquatic plants: IC50 (Pseudokirchneriella subcapitata (green algae)): 5.6 mg/l Exposure time: 72 h Method: OECD Test Guideline 201

**Titanium dioxide:**
- Toxicity to fish: LC50 (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l Exposure time: 96 h Method: OECD Test Guideline 203
- Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): > 100 mg/l Exposure time: 48 h
- Toxicity to algae/aquatic plants: EC50 (Skeletonema costatum (marine diatom)): > 10,000 mg/l Exposure time: 72 h
- Toxicity to microorganisms: EC50: > 1,000 mg/l Exposure time: 3 h Method: OECD Test Guideline 209
Persistence and degradability

Components:

Cellulose:
Biodegradability: Result: Readily biodegradable.

Bioaccumulative potential

Components:

Amlodipine Besylate:
Partition coefficient: n-octanol/water: log Pow: 3

Mobility in soil
No data available

Other adverse effects
No data available

Section 13: Disposal considerations

Disposal methods
Waste from residues: Dispose of in accordance with local regulations.
Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal.
If not otherwise specified: Dispose of as unused product.

Section 14: Transport information

International Regulations

UNRTDG
Not regulated as a dangerous good

IATA-DGR
Not regulated as a dangerous good

IMDG-Code
Not regulated as a dangerous good

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

National Regulations

NZS 5433
Not regulated as a dangerous good

Section 15: Regulatory information

Safety, health and environmental regulations/legislation specific for the substance or mixture
HSNO Approval Number
HSR100425 Pharmaceutical Active Ingredients Group Standard 2017

HSW Controls
Certified handler certificate not required.
Tracking hazardous substance not required.
Refer to the Health and Safety at Work (Hazardous Substances) Regulations 2017, for further in-
formation.

The components of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined

Section 16: Other information

Further information

Date format : dd.mm.yyyy

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
NZ OEL : New Zealand. Workplace Exposure Standards for Atmospheric Contaminants

ACGIH / TWA : 8-hour, time-weighted average
NZ OEL / WES-TWA : Workplace Exposure Standard - Time Weighted average

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect